
REPORT:

Agreement on Mutual Recognition

Between the United States Food and Drug Administration and the European Union – Concerning Industry and Public Health

Docket Number: 98S-1064

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This published report is intended to provide consumer groups, trade associations and legislators with the latest information regarding recent developments on the Mutual Recognition Agreement (MRA) between the United States and European Union. Many of these findings resulted from researching public records, and correspondence with various stakeholders at the FDA, US Dept. of Commerce and United States Congress. Names have been included to provide opportunities to verify assertions that are otherwise undocumented. Wherever supporting documents exist, they have been referenced. While this report details trade, health and safety concerns, it is not intended to undermine the attempts by concerned government agencies, especially the FDA, to develop what may eventually become a solution for differences that presently exist between government regulatory systems. This report focuses mainly on international quality system and medical device regulations.

The author of this report wishes that all those people cited in this report be given the utmost respect for their hard work and determination to overcome the very complicated task of balancing trade with public health.

The MRA - What is currently agreed to:

- 1) The U.S. has agreed to harmonize its quality system (21 CFR Part 820) regulation with the European Union.

“Therefore, FDA has worked closely with the GHTF and TC 210 to develop regulation which is consistent with both ISO 9001:1994 and ISO/CD 13485.”

- [Docket No. 90N-0172 page 52605]

- 2) The FDA will allow European Notified Bodies NB's [now referred to as Conformity Assessment Bodies or CAB's] to perform FDA inspections to US requirements.

“...10 U.S based Conformity Assessment Bodies (CAB's) will function essentially as Notified Bodies. However, the U.S. CAB's will not have the final responsibility for assigning the [European Certification] CE mark”

- John Stigi - FDA Director of Small Manufacturers Assistance: date December 6, 1999

The MRA - What is NOT agreed to:

- 1) The Europeans will not accept FDA inspections conducted by the FDA's Office of Compliance in any way, shape or form, even though the inspection criteria are identical and the method of inspection is well documented in the FDA's "Quality System Inspection Technique" (QSIT). The European's refuse to allow any FDA conducted inspections to carry any weight when determining compliance with the European System.

“There is no current reciprocity for FDA inspections and [Notified Body] NB audits.”

- Letter from John Stigi dated December 6, 1999.

- 2) A Harmonized Risk Classification system does not exist. This is critical to determining which regulations apply to a particular product. Class 2 (Medium risk) devices in one country may not be "Exempt" from particular requirements that apply to a class 1 (Low risk) device. An example of these risk classification differences is illustrated on the last page of this report. The sample device shows how dental drills are class 1 in the US and class 2 in Europe. Are US devices under-regulated or are European devices over-regulated.

“We are more than aware of the differences in the U.S. and E.U. [Risk] classification systems. Since country specific classification systems (US, EU, Japan, China, etc.) are not harmonized, there is nothing we can do to correct the problem.”

- John Stigi

What is the purpose of having an agreement?

Following interviews with several MRA stakeholders working for both the FDA and US Department of Commerce, it appears that not enough attention has been given to critical areas of this MRA. There continues to be a significant amount of pressure to put the current agreement into affect, despite flaws, which undermine the principals for having it. The MRA was designed without significant involvement from U.S. industry. The resulting “agreement” does not offer anything new to US industry that it does not already have. Another shortcoming is the lack of agreement on the risk classification of certain medical devices.

Before a company can determine which regulations apply to its product, it must first identify its “risk class”. Though somewhat subjective, nearly all countries use a risk classification based regulatory scheme. Products that are life supporting are subject to more controls than those that provide a mild therapeutic affect. Most countries agree that Pacemakers are considered class 3 (high risk) and should be more regulated than dental floss, which is class 1 (low risk). Since the MRA does not take into consideration the US risk classification scheme, US manufacturers are forced to adopt the European’s. The European system for classifying devices is so vague that additional guidance documents must often be purchased or sought out. After determining what the CE marking requirements are, US manufacturers often find themselves wondering how they’re going to find the money to pay for CABs. CE marking directives do not require CAB surveillance in Europe for class 1 devices. However, companies who rely on the FDA classification systems or inspections would be in violation of European Law if they were to try and utilize either of them. There is no agreement on these two critical issues.

An example of the particularly crippling affects that are resulting from the MRA can be seen in the Dental manufacturing industry. Here in the US, they are subject to biannual FDA inspections for their class 1 devices. The European Union refuses to acknowledge either the US classification scheme or inspections conducted by FDA personnel. Dental systems are considered class 2a in Europe and are subject to costly privatized CAB surveillance.

Does the MRA improve public health and safety?

The proposed privatization of surveillance by using CABs, fails to provide any benefit to US manufacturers and threatens public safety since this third party review systems have been statistically proven to be ineffective at satisfying the requirements for safety that is mandated by the FDA. As stated earlier, the FDA’s Quality System Regulation (QSR) has been harmonized with the ISO 9001 and 13485 standard by the same technical committee (TC 210) that wrote these standards. Yet:

“21% of European Manufactures fail their FDA quality system audits – all of them were ISO certified”

- Wes Morgentstern – FDA CDRH, Office of Compliance

Why do FDA auditors find so many CAB auditors not doing their jobs? All CABs are third party ISO type quality system registrars. Does the MRA expose the general public to a 20% increase in risk by accepting CAB surveillance in place of FDA inspections? The FDA’s office of compliance believes the MRA ignores public safety concerns.

If the Europeans have designated the FDA as a suitable authority for selecting and training quality system auditors, why will they not acknowledge the suitability of a quality system inspection conducted by the FDA’s enforcement office?

Additional US public safety concerns exist because the Competent Authorities (EU Government Health Ministries) are responsible for policing CABs and industry in Europe to ensure that acceptable FDA inspections are conducted on behalf of US public citizens. Their apparent lack of participation in FDA Quality System training indicates a serious problem for U.S. consumers. If the individual EU states were so concerned about the FDA's quality system methods and public safety why did every Competent Authority ignore their invitation to send a representative to the FDA's quality system training in Europe? There seems to be no indication that these E.U. government agencies will provide suitable monitoring of E.U. CABs. [Ref. MRA Stakeholders Meeting June 27, 1999]

Conflict of interest cannot be eliminated

The FDA realizes that there is a potential problem with conflict of interests

“FDA will expect CABs to be impartial and free from any commercial, financial, and other pressures that might present a conflict of interest or an appearance of conflict of interest.”

- FDA Guidance for Staff, Industry and Third Parties. Page 9

What is a CAB? It is a company that is paid money by a manufacturer to perform an audit to determine compliance with the requirements of particular quality system regulations. The CABs sell their inspection services and if a manufacturer is dissatisfied with the “CAB services”, they may be fired. This happens frequently. There are incidences from all over the world where ISO registrars have compromised their audits in order to achieve their own economic goals. There are already several companies that have been selected as CABs that are under investigation for violating conflict of interest requirements. It is a consistent problem that requires constant policing from the Competent Authorities.

In contrast, FDA personnel have no financial stake in whether a company passes or fails an audit. The government pays them, and the results of their findings are driven by the safety and health concerns of the taxpaying public who ultimately finance these inspections. Manufacturers can't fire them if they don't like the outcome of the FDA inspection. The FDA inspection is still the most respected and feared audit on the planet. FDA inspections are better than privatized CAB surveillance since the FDA works without any conflict of interest.

What is the driving force behind the MRA?

Ironically, on behalf of the Clinton Administration, the US/EU MRA is being driven by the US Department of Commerce and not the FDA, as some might believe. The US DOC who is supposed to be improving trade for US companies is actually supporting a system that does nothing for them at all. On two separate occasions, FDA personnel (Mr. John Stigi and Ms. Chris Nelson) said that they had no choice but to adopt the MRA because they were under enormous pressure from the US DOC and the Clinton Administration to “get it done quickly”. The European Commission has held it's ground, preventing the FDA from preparing an agreement that would better serve U.S. interests. The MRA is not about public safety. It is about trade and about privatizing the regulatory activities of our governments. The FDA's Dental Division office confided that EU dental manufacturers felt they were at a competitive disadvantage having to pay for costly third party surveillance that the US manufacturers were not yet subjected to. Taxpayers pay for FDA audits.

Does the European Union care as much about U.S. public health as Americans?

When the FDA held its quality system training in London on June 21-25, Ms. Chris Nelson of the FDA's Office of Compliance stated there were 36 attending representatives from 12 EU CABs. Health ministries from the EU ignored their invitations to attend. CABs saw this training as a necessary part of advancing their commercial interests. John Stigi, in an attempt to get the MRA going, furthered the ambitions of these EU CABs by promising to distribute 1900 FDA mailers to E.U. manufacturers, advising them to hire these CABs, rather than of having to rely on FDA inspectors. [Ref. MRA Stakeholders Meeting June 27, 1999]

How much has this cost? How much will it cost?

The economics of creating an MRA is difficult to measure. Although the FDA has developed some figures regarding the cost of their activities (not yet disclosed to the public), there are significant concerns with the agreement's long-term impact on industry and consumer prices. Simple math can be used to estimate the economic impact for implementing third party quality system surveillance by CABs.

- 1) The average cost of an initial inspection is roughly \$10,000 US Dollars. If everyone on John Stigi's list adopts the MRA, they will spend \$19 million during the first year.
- 2) Each annual follow-up audit costs roughly \$5000 for an annual cost of 8.5 million US Dollars.

These figures are a little lower because European based CABs often charge less than their American offices charge. This is in direct contrast to what many American companies have been led to believe. Some US offices representing CABs based in the UK charge over \$20,000 for the first audit and \$7,000 to \$8000 for each follow-up audit. Some of these audits are conducted every 6 months. [Estimates provided by CABs (G-MED, SGS, BSI, UL and LRQA) for an ISO 9000 equivalent quality system audit, of a company with 50 employees, at one location]

Will US manufacturers save time and money by using CABs based in the US?

Some FDA officials state that there is a "logistical benefit" to using US based CABs verses EU notified Bodies to get the CE mark. This is patently untrue for several reasons:

- 1) There are always "travel fees". If the CAB is located in the US, he will likely have to fly to the manufacturer's location, rent a car and stay at a hotel. The only difference is in the airline ticket price, which never varies by more than \$500. This nominal difference is easily eliminated by telling the Notified Body to lower their price.
- 2) The United States is a market driven economy. CABs have been competing against each other for US business ever since the CE marking directives went into affect in Europe. The MRA cannot take credit for this natural progression. It could be argued that the MRA may actually reduce competition by inferring that one of the ten selected US CABs be used in place of one of the more than 20 European Notified Bodies who already offer similar services.
- 3) Manufacturers will find it less expensive to use a good Authorized Representative in Europe to solicit competitive bids directly from European Notified Bodies. This will save the US manufacturer the most money. US based CABs charge 10% to 50% more to cover administrative costs that are not normally charged by their European counterparts. The E.U. has also established limits as to how much a notified body can charge in Europe.
- 4) US CAB audit reports must still be processed through the Notified Bodies in Europe under the current MRA. US manufacturers may save time and money if they hire a EU Notified Body instead of a US based CAB.

One would think that these oversights in the implementation of the MRA might have been anticipated. Perhaps the lack of transparency with the general public and industry was a contributing factor. Perhaps pressure to "get it done" meant adopting regulations that the European Commission would not change. Examine the quoted "objectives" of the MRA. that were stated to the United States Congress by a top FDA representative on October 2nd of 1998. How has the FDA done over the last 24 months?

Quoted from FDA statement to Congress, Sharon Smith Holston October 2, 1998

“FDA's objectives for the MRA, as developed in our internal discussions, were to:

- 1. Enhance FDA's ability to ensure that the health and safety of American consumers are protected;*
- 2. Obtain the information necessary to determine whether the EC Member State regulatory systems for GMPs are equivalent to FDA's;*
- 3. Establish enhanced communications between FDA and the Member State regulatory authorities concerning the quality of pharmaceutical products exported to the U.S.; and*
- 4. Eliminate unnecessary regulatory burdens on industry.”*

Is the MRA satisfying the FDA's objectives?

- Point 1: Not only is the MRA's acceptance of CABs a questionable method of ensuring public health and safety, but even more concerning is the apparent lack of participation of Competent Authorities in activities essential to enforcement. Since the MRA relies on EU Competent Authorities who appear unwilling or incapable of policing EU CABs, American consumers are not adequately protected.
- Point 2: The FDA adopted a quality system that was harmonized with the Europe's, however, a risk classification systems is not agreed to. What products are exempt from which regulations? Risk Classification is at the top of this pyramid in both regulatory systems.
- Point 3: If a vigilance system for adverse event reporting is established between the E.U. and FDA, public safety would be enhanced.
- Point 4: US industries will not benefit from the MRA. The fact that the United States did not insist that its FDA inspections should be considered as equal to a CAB inspection was a big mistake, particularly since very small manufacturers cannot afford the start-up and maintenance fees associated with CAB surveillance. Given that many US firms may already have had an FDA inspection and certification to the FDA's harmonized Quality System Regulation (21 CFR Part 820), why wasn't it negotiated? Australia's government did not miss the opportunity to help their industry. Australia's Therapeutic Goods Administration (TGA) decided they will be Australia's CAB. The FDA and US DOC must consider this also.

The US DOC must take responsibility for pushing the FDA into an agreement that does not meet the intentions set forth in Congressional Hearings. The US DOC is currently preparing a document outlining the benefits of the MRA for US firms. I imagine the only firms that will be excited will be CABs. It is disturbing that nothing will be provided to the U.S. public that will give them the same level of optimism.

Reported by:

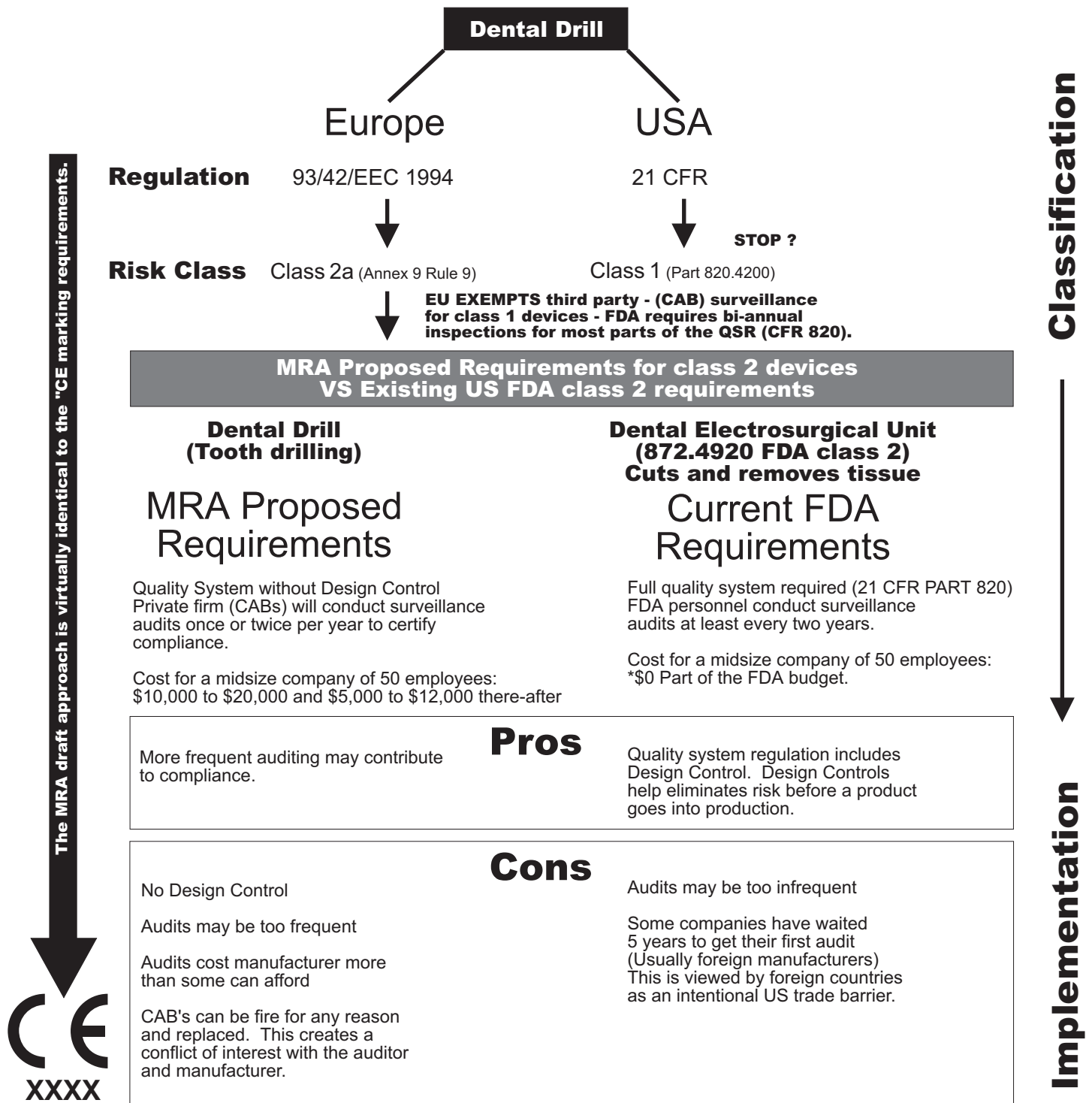
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Risk Classifications and Route to Conformity Differences between the USA and E.U.



Dental drills are only one device example of many that are exempt from third party inspections in one region but NOT exempt in another. The MRA does not address how these device risk classification differences are to be handled.

Companies selling FDA class 2 devices save thousands of dollars in surveillance fees by utilizing the FDA personnel and free surveillance audits. The Current Good Manufacturing Practice 21 CFR Part 820 is harmonized with the quality systems of Europe and the rest of the world. The European Union refuses to acknowledge FDA inspections as being equivalent, even though they acknowledge the substantial equivalency to their own quality system requirements in 93/42/EEC.